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Shelley P.M. Fussey, Ph.D.
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Dear Shelley:

We would like to place on record the concept of an invention.

We envision a method for targeting drugs, coagulants or imaging agents to tumor blood vessels for tumor therapy or imaging. Annexins (e.g. annexin V) are a family of human proteins that bind with high affinity (Kd = 7nM) to phosphatidylserine, a simple phospholipid that becomes exposed on the surface of activated cells (platelets and nucleated cells) and on apoptotic or injured cells. Several factors known to be present in tumors lead us to expect that annexins would home selectively to tumor vascular endothelium after systemic administration. These factors include; i) activation of endothelial cells by cytokines released by tumor cells and infiltrating host cells; ii) death or apoptosis of endothelial cells in tumors due to oxygen starvation or physical compression; iii) apoptosis of endothelial cells in tumors due to vascular remodeling which is believed to involve endothelial cell death as well as endothelial cell migration and proliferation; iv) deposition of and activation of platelets on tumor vessels and binding of annexins to the bound platelets. None of these factors is likely to be as prominent in the vessels of normal tissues. If annexins localize selectively to tumor endothelium, it should be possible to make chemical constructs between annexins and drugs or coagulants. It should also be possible to fuse the genes encoding annexins and cytotoxic proteins (e.g. diphtheria toxin, ricin) or coagulant proteins (e.g. tissue factor, factor Xa, thrombin). Such agents might be useful for modulating or thrombosing tumor vasculature. Similarly, radionucleides or imaging agents might be attached to annexins to produce reagents for imaging tumor vasculature.

These concepts were conceived jointly by us without inventive input from other people.

Yours Sincerely,

Philip E. Thorpe

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